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Letter to the Editor

Pediatric high-grade glioma resources from the Children's Brain Tumor Tissue Consortium

Pediatric high-grade gliomas (pHGGs) are a leading cause of pediatric cancer death but are genomically and spatially distinct.^{1,2} In this report we describe the generation and characterization of pHGG reagents with linked genomic and longitudinal clinical data freely available to the community to accelerate pHGG research.³

The pHGG biospecimen collection, annotation, genomic sequencing, and cell line generation were coordinated by the Children's Brain Tumor Tissue Consortium (CBTTC) (<https://cbttc.org>), which is an international, collaborative, multi-institutional research program dedicated to the study of childhood brain tumors. After project proposal approval, the specimens are delivered to investigators while CBTTC data are available for viewing and download from the Gabriella Miller Kids First Data Resource Center (KF-DRC, <https://kidsfirstdrc.org>) or as processed data in PedcBioPortal (<https://pedcbiportal.org>). All subjects consented to tissue and data collection through CBTTC Institutional Review Board–approved protocols. The KF-DRC is recognized as a National Institutes of Health Trusted Partner for data sharing protections.

The CBTTC cohort of pHGG primary tumors represents the spectrum of disease. The clinical covariates, genomics, and biospecimens of the pHGG set in this study are shown in Figure 1. The cohort with tumor whole genome sequencing represents 73 participants. Tumors were from participants with a median age of 9 years at diagnosis and 55% were female. Sixty percent were from initial or diagnostic specimens and 46% were from a hemispheric location. Analysis of a selected set of recurrently mutated pHGG genes was of an expected distribution with 47% *TP53*, 36% *H3.3*, 24% *ATRX*, and 7% *BRAFV600E* variants.² Tumors had mutually exclusive *H3.3* G34 and K27M mutations and co-occurring mutations of *ATRX* with *H3.3* G34R or *NF1*.^{4,5} Seven participants' tumors demonstrated features of hypermutation with somatic and/or germline mismatch repair deficiency.⁶

At the time of study initiation, the CBTTC biorepository had 37 pHGG tumor tissues stored in freezing media that were dissociated and cultured with 4 different culturing conditions. At least one culture grew from 23/37 (62%) dissociation events from 23/73 (31%) patients in our cohort. Patient derived cell line information including prior patient therapy, culture, and growing conditions, including orthotopic xenografts, doubling times, and validation status are described elsewhere.³ The cell line panel represents the spectrum of pHGG genomics with 8 unique patient cell lines with *H3.3* mutations (35%), 6 with *TP53* mutations (26%), 1 with a *BRAFV600E* mutation, and 1 with a

KRAS Q61H mutation. Three patient cell lines were derived from tumors with mismatch repair deficiency and hypermutation.

For each of the tumors in the CBTTC there are additional banked biospecimens including tumor tissue, tumor in freezing media, blood, plasma, cerebrospinal fluid, and both tumor and blood derived nucleic acids (<https://cbttc.org>). Of the pHGG cohort in this study, 36 patient tumors are also available on a tissue microarray. This valuable resource will enable researchers to examine the tumor microenvironment, discover cell surface immunotherapy target proteins, or perform validation studies of the corresponding proteomic dataset. Finally, to facilitate integrative studies, most of the tumors in the pHGG set have corresponding redacted operative reports and pathology and radiology reports, along with the relevant MRI images and histology slides. Supplementary Figure 1 shows reagents for patient PT_9BZETMOM (7316-158 and 7316-5317), whose diagnosis and relapse tumors have the rare *H3.3* G34R mutation.

In summary, the CBTTC with its member institutions, donors, patients, and families has developed an infrastructure to support pHGG research for both large genomic projects and individual laboratories. The CBTTC pHGG patient tumors and associated datasets are expected to increase, which when integrated with adult cancer and other disease sets promise to advance discoveries and hope of effective therapies for this devastating disease.

Supplementary Material

Supplementary data are available at *Neuro-Oncology* online.

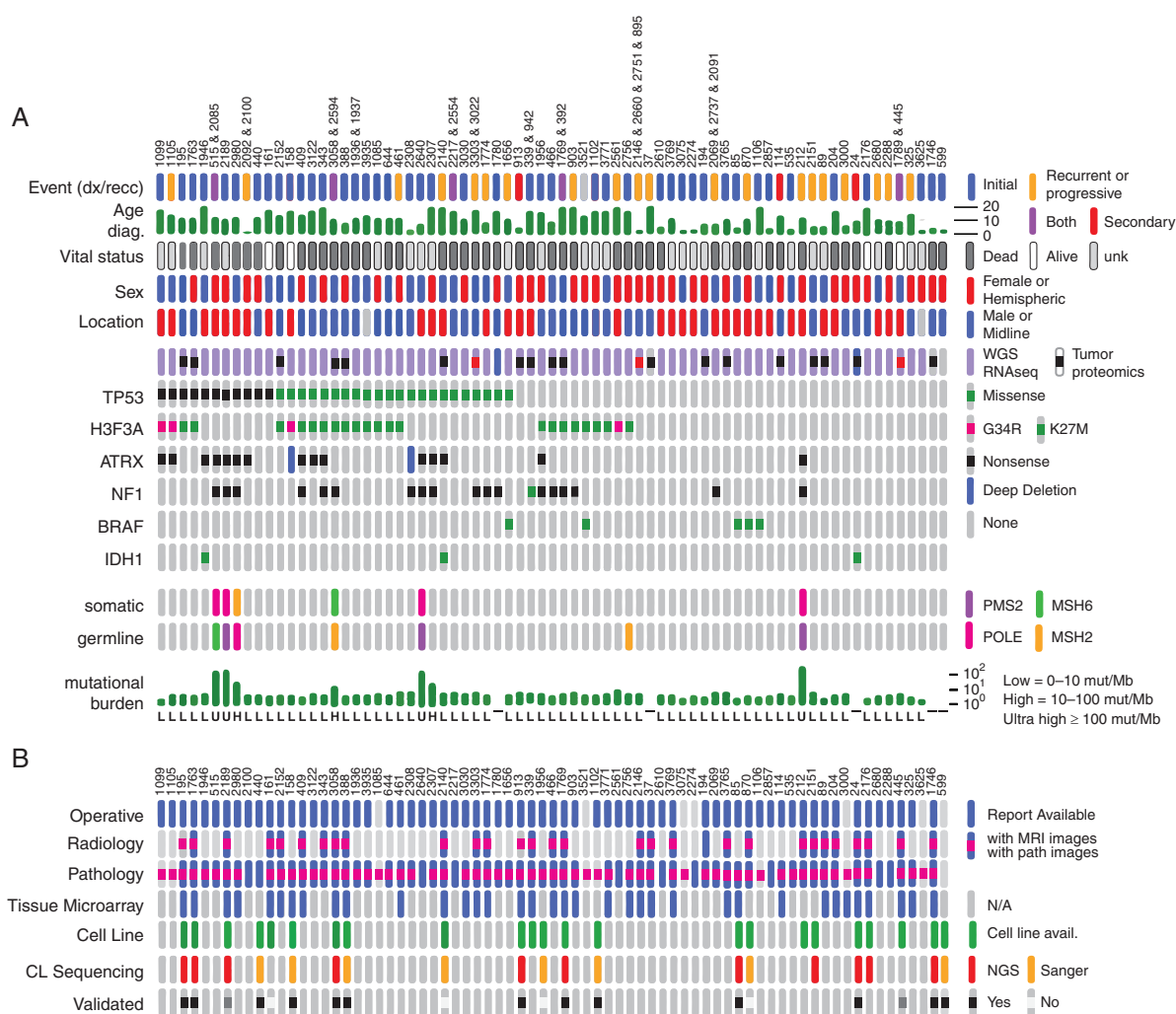
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Conflict of interest statement. None.

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The CBTC pHGG cohort. OncoPrint of the clinical covariates, genomics, and resources of the pHGG cohort. dx = diagnosis; recc = recurrence; NGS = next generation sequencing of cell lines.

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